REMARKS

This paper is being filed in response to the Office Action dated May 29, 2003. Applicants respectfully request reconsideration of the above-identified application in light of the amendments and remarks presented herein.

Claims 44-48, 65-69, 121, and 133 are pending. Claim 44 has been amended. Support for the amendment can be found throughout the specification and claims as originally filed, in particular at pp. 13-14, ¶¶ 34-35. Claim 48 has been amended to correctly define the subject matter. Claim 69 has been amended to correct a typographical error. Support for the amendment to claim 69 is found at page 15, ¶ 37. No new matter has been introduced by the amendments to the claims.

Rejection Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 69 under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner notes that "MIP-3y" is vague and indefinite as the term is not defined in the specification. In response, Applicants have amended claim 69 to correct the typographical error from "MIP-3ÿ" to "MIP-3β." Support for this amendment is found at page 15, ¶ 37. The MIP-3β is the specific chemotactic factor elected in the Response to Incomplete Reply mailed March 12, 2003. Therefore, Applicants submit that claim 69 properly point outs and distinctly claims the subject matter which applicant regards as

the invention. Applicants respectfully request withdrawal of the rejection of claim 69 under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 44-48, 65, 66, 69, 121, and 131 under 35 U.S.C. § 103(a) as being unpatentable over US 5,817,343 (Burke) in view of Kim et al. The Examiner alleges that Burke teaches a method for providing an artificial gradient in vivo comprising administering an ethylene-vinyl-acetate device subcutaneously, said device comprising a chemotactic factor such as a chemokine, wherein the administration is useful for the controlled or sustained release of drugs. The Examiner alleges that the difference between Burke and the claimed invention is the absence of the disclosure of MIP-3β. The Examiner alleges that Kim et al. teach that MIP-3β is a strong chemoattractant for T cells and mature B cells. In addition, the Examiner alleges that it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to provide an artificial chemotactic gradient in vivo comprising administering an ethylene-vinyl-ethylene device subcutaneously, said device comprising a chemotactic factor, said factor comprising a chemokine as taught by Burke and substituting the specific chemokine MIP-3β as taught by Kim et al. The Examiner contends that one of skill in the art would have been motivated to use the specific chemokine because MIP-3β is a strong chemoattractant for T cells and mature B cells and thus would prove useful in a controlled or sustained release device used in the treatment of any disease for which the attraction of T or B cells might prove useful, for example, essentially any pathogen-mediated disease or cancer. Applicants respectfully disagree.

As set forth in *Graham v. Deere*, a finding of obviousness under 35 U.S.C. § 103 requires a determination of the scope and content of the prior art, the level of skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. John Deere, Inc.*, 383 U.S. 1 (1966). The art must provide both the suggestion and a reasonable expectation of success. *In re Vicki*, 947 F. 2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The prior art reference(s) must teach or suggest all the claim limitations. Both the suggestion and a reasonable expectation of success must be present in the references.

The present invention relates to an artificial chemotactic factor gradient created *in vivo*, which can be used to entrap dendritic cells circulating through a subject's bloodstream. Furthermore, claim 44 has been amended to include the limitation "wherein transient entrapment of antigen presenting cells is achieved." The entrapped cells can be manipulated *in situ* for therapeutic purposes. For example, these cells can be loaded with one or more immunoregulatory molecules, such as a tumor-associated or infectious disease-associated antigen. Thus, the therapy lies within the use of the cells entrapped within the subject's body by the artificial gradient created by the administration of the chemotactic factors to carry out the required treatment. Thus, the therapeutic agent is not the chemotactic factor itself.

In contrast, Burke does not disclose an artificial chemotactic factor gradient *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Burke teaches a method of

formulating slow release particles for drug delivery comprising forming a polymer solution/drug mixture in a solvent, removing the solvent from the mixture to form a solid matrix, and fragmenting the matrix at a temperature below the glass transition temperature of the matrix. In contrast to the present invention, Burke discloses the possibility of delivering a chemokine as the therapeutic agent. There is no mention of manipulating entrapped cells as agents to carry out a required therapy. There is also no mention of the use of the device disclosed in Burke for the treatment of any disease for which the attraction of T or B cells might prove useful. In addition, Burke provides no suggestion or motivation for the creation of an artificial chemotactic factor gradient *in vivo* to transiently entrap antigen presenting cells.

Kim et al. does not teach an artificial chemotactic factor gradient *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Kim et al. describes the pharmacological activity of MIP-3β to attract T and B cells. There is no mention of the creation of an artificial gradient to entrap antigen presenting cells. Furthermore, there is no suggestion or motivation provided by Kim et al. to create such an artificial gradient to entrap antigen presenting cells.

Neither of the references teach, alone or in combination, all the required limitations of the amended claims, i.e. a method for providing an artificial chemotactic factor gradient *in vivo* comprising administering a composition comprising one or more chemotactic factor(s), wherein transient entrapment of antigen presenting cells is achieved. Furthermore, there is no suggestion or motivation to combine the cited references to produce the presently

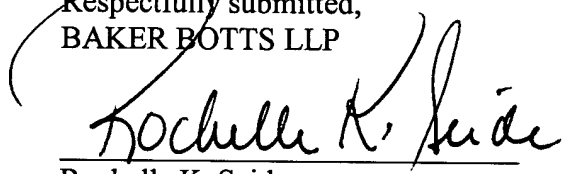
claimed method, and thus there is no reasonable expectation of success. Therefore, applicants respectfully request the withdrawal of the rejection of claims 44-48, 65, 66, 69, 121, and 131 under 35 U.S.C. § 103 (a).

CONCLUSION

Based on the foregoing amendments and remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is respectfully requested.

Applicants believe no fee is required for this submission. Should any fee be due or overpayment made in connection with the submission of this paper, the Commissioner is hereby authorized to charge such fees or credit the overpayment to Deposit Account No. 02-4377. A duplicate copy of this page is enclosed.

Respectfully submitted,
BAKER BOTTS LLP



Rochelle K. Seide
Patent Office Reg. No. 32,300

30 Rockefeller Plaza
New York, NY 10112-4498

Attorney for Applicants
(212) 408-2500